

claims do not introduce new subject matter and are supported in the specification and the claims as originally filed, their entry is respectfully requested.

**Objections and Rejections Under 35 U.S.C. § 112, Second Paragraph**

Claims 53-57 and 66-69 stand rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. Claims 53-57 have been amended to correct an improper antecedent basis for the phrase "said encoded polypeptide" by deleting the phrase and replacing it with the phrase "said isolated nucleic acid encodes a polypeptide which" as suggested by the Examiner. Claim 66 has been amended to depend from Claim 53 rather than from cancelled Claim 1. In light of the amendments to the claims and the discussion above, Applicants respectively request reconsideration and withdrawal of the outstanding rejections under 35 U.S.C. § 112, second paragraph.

**Rejections Under 35 U.S.C. § 101**

Claims 53-69 stand rejected under 35 U.S.C. § 101 for allegedly lacking a credible, specific and substantial asserted utility or a well established utility. The Examiner has stated that it is unclear from Example 13 of the specification that the "universal normal control" is an appropriate control. However, the Examiner has indicated that the new data from parallel and concurrent studies that was submitted by Applicant in their response to the January 17, 2003 Office Action may be probative of the utility of the claimed invention. Yet, such new data is more properly presented in the form of a declaration under 37 C.F.R. § 1.132. Applicants herein provide the Declaration of Thomas D. Wu, M.D., Ph.D., wherein Dr. Thomas D. Wu declares that in addition to using the above described "universal normal control" in these microarray studies, parallel studies were concurrently conducted. In these contemporaneous studies, the level of expression of the PRO3301-encoding nucleic acid sequence was compared in both tumor samples and in control samples of the same tissue type as the tumor samples

examined. These concurrent studies demonstrated that compared to their normal healthy tissue counterparts, PRO3301-encoding nucleic acid sequences showed, on average, a 2.4 fold, 9.2 fold, and 5.3 fold increase in expression levels in non-small cell lung adenocarcinomas, lung squamous cell carcinomas, and colorectal adenocarcinomas, respectively. These results demonstrate that PRO3301-encoding nucleic acid sequences are significantly overexpressed in specific tumor tissue(s) when compared to their specific normal tissue controls and thus can be useful as a diagnostic marker for the presence or absence of such specific tumor(s) in a tissue sample of unknown pathology. As such, the PRO19598 polypeptides encoded by the claimed polynucleotides have patentable utility in their being able to bind/label PRO3301 in cancer diagnostic assays.

Applicants respectfully request the acceptance into evidence Dr. Thomas D. Wu's Declaration submitted herein under 37 C.F.R. § 1.132. In light of this declaration, amendment to the claims and the discussion above, Applicants respectfully request reconsideration and withdrawal of the outstanding rejections under 35 U.S.C. § 101.

**Rejections Under 35 U.S.C. § 112, First Paragraph**

Claims 53-69 are rejected under 35 U.S.C. § 112, first paragraph for allegedly lacking

a credible, specific and substantial asserted utility or a well established utility for the same reasons outlined in the rejections under 35 U.S.C. § 101. Applicants have herein provided the Declaration of Dr. Thomas D. Wu under 37 C.F.R. § 1.132 to provide evidence and support for Applicants' assertion that the claimed invention is supported by a credible, specific and substantial asserted utility or a well established utility so that one skilled in the art would know how to use the claimed invention. In the light of this declaration and the arguments and discussion traversing the rejections under 35 U.S.C. § 101, Applicants respectfully submit that specification discloses a credible, specific and substantial utility for the claimed invention as useful diagnostic tools for detection of lung and colorectal tumors.

In addition, Claims 64-69 are rejected under 35 U.S.C. § 112, first paragraph for allegedly reciting a genus of polynucleotides without indicating functional limitations. The Examiner has stated that Claims 53-63, as previously amended recite structural and functional limitations for the encoded polypeptides resulting in an adequate written description of a claimed genus. Applicants have herein amended Claims 64 and 66-67 to provide the functional limitation "wherein said isolated nucleic acid encodes a polypeptide which is a receptor for and binds to the ligand polypeptide shown as SEQ ID NO:4" in order to provide an adequate written description of the claimed genus. Thus, the genus claims, as amended, recite a specific utility for the claimed variant nucleic acids which encode a polypeptide which is receptor for and binds to a functional ligand polypeptide. Since the claims are now drawn to a genus defined by both sequence and functional identity, one of ordinary skill in the art would know at the effective priority date of this application, that the Applicants were in possession of the claimed sequences.

In view of the Declaration of Dr. Thomas D. Wu submitted herewith, amendments to the claims and the discussion above traversing the rejections under 35 U.S.C. §§ 101 and 112, Applicants respectfully submit that the specification discloses a credible, specific and substantial utility for the claimed invention as useful diagnostic tools for detection of lung and colorectal tumors. Accordingly, the Examiner is respectfully requested to reconsider and withdraw the rejections of the claims under 35 U.S.C. § 112, first paragraph.

In light of the above amendments and remarks, Applicants believe that this application is now in condition for immediate allowance and respectfully request that the outstanding rejections be withdrawn and this case passed to issue.

The Examiner is invited to contact the undersigned at (650) 225-4563 if any issues may be resolved in that manner.

Respectfully submitted,

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